

## SPARING EFFECT OF NEUROLOGICAL DEFICIT AND TRAUMA ON THE COURSE OF ADJUVANT ARTHRITIS IN THE RAT\*†

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The distribution of joint involvement in arthritis of various types, in relation to neurological impairment of a limb, has been the subject of interesting clinical observations. Our observation of an apparent example of an altered pattern of joint involvement in arthritis following tendon laceration prompted a series of experiments. These experiments were devised to evaluate the effects of induced neurological and functional impairments on the distribution and extent of adjuvant arthritis in the rat.

Recently Thompson and Bywaters (1962) reviewed the protective effect of previously occurring hemiplegia on joint involvement in rheumatoid arthritis. They also reported the sparing effect of previously occurring Erb's palsy on the distribution of Heberden's nodes. Hench (1940) had reported similar observations. Thompson and Bywaters found the protection after hemiplegia not absolute but likely. On the other hand, Nava (1953) reported a severe exacerbation of a mild rheumatoid arthritis resulting in joint involvement only on the side involved by a subsequent hemiparesis. More recently, Haddad (1963) has described the possible sparing effect of fracture of the humerus, with bony non-union, but long usage, in a patient with osteo-arthritis.

In two of Thompson and Bywater's rheumatoid patients, who were ambulatory for many years in spite of previous hemiplegia, arthritis did not appear on the affected side. In a sense, these patients were using their limbs, but they did not enjoy complete usefulness because of the absence of fully-integrated

information loops.\* They noted little difference in circulation between the hemiplegic and arthritic limbs. Furthermore, they observed no vascular differences in the distribution of macroglobulins. They did, however, indicate the probability of some direct change in the joints possibly consequent upon both lower and upper motor neuron injury.

### Case Report

A female patient aged 81 had lacerated the flexor tendon of the fourth digit of the left hand at age 33. The tendon remained severed. At age 40, she experienced an episode of probable rheumatoid arthritis of moderate severity which lasted several years. At about age 70 she began to suffer from a severe generalized osteo-arthritis and was treated elsewhere with 20 to 40 mg. hydrocortisone per day for 9 years. At age 81, 11 years later, she presented herself at our clinic with a painful arthritis involving the hands, knees, and ankles.

At that time the laboratory findings were as follows: Haematocrit 42 mm.; Erythrocyte sedimentation rate (Wintrobe) 25 mm./hr; serum uric acid 2.7 mg./100 ml.; latex-fixation test negative; normal urine analysis.

X-ray studies showed "marked narrowing of the articular cartilages of many of the small joints of the hands and wrists bilaterally, involving most severely the proximal interphalangeal joints of the second, third, fifth fingers of the right hand, the distal interphalangeal joints of all save the left fourth finger, and the interphalangeal joints of the thumbs. Considerable hypertrophic secondary change is present about the majority of the severely involved joints and is also noted about the multangular joints of the left wrist. Moderate osseous

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\* Involved in the regulation of function is the concept of information theory. This notion is also related to control and communication through information loops. The theory of self-regulation may apply both to mechanical and physiological phenomena. In models simulating biological systems, information loops may be classically considered to extend from neurological receptors centrally to control centres, returning peripherally again to affect vascular and metabolic responses, and then from these phenomena back again to both neurological and psychical control centres. Negative feedback through the loop may dampen the subsequent responses if they are increasing, and positive feedback may increase the subsequent responses to engender a runaway pathological condition (Shannon and Weaver, 1949).

demineralization is noted. Impression: Advanced arthritis of the small joints of both hands and wrists (with sparing of the left fourth digit), predominantly rheumatoid in type with considerable superimposed hypertrophic changes about the more severely involved joints."

Thus, all the digits except the left fourth showed clinical and roentgenological evidence of arthritic changes (Fig. 1).

*Examination.*—Accurate response was elicited, with eyes closed, to light and touch and pin-prick stimuli over the spared finger. Subjectively, the patient felt that sensation was somewhat impaired on this digit.

When tested with an occlusion plythysmograph,\* the

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spared fourth digit revealed a flow of 7.5 mm./4 ml. vol./sec., while the pulse waves were 4 mm. in height (calibration 10 mm.) and were of flattened configuration. The arthritic third left digit showed a flow rate of 10 mm./4 ml. vol./sec., and the pulse waves were 6 mm. in height and characterized by a normal anacrotic limb and diastolic notch.

Temperature measurements of the finger tips were made when the ambient temperature was 22.2° C. The fingertip skin temperature of the left fourth finger was 29.8° C. while those for the other finger-tips were: first—33.8°, second—32.0°, third—31.2°, and fifth—32.0° C.

The Allen test showed normal rebound following occlusion for 1 min.

Several details in this patient's history may eventually be regarded as of other than incidental interest to the



Fig. 1.—X-ray study demonstrating possible sparing effect of previous flexor tendon section on arthritic involvement of the fourth digit of the left hand.

course of the arthritic involvement, although presently there is no clear relationship among them. The patient's mother and brother both had pulmonary tuberculosis at age 30 and both died at age 62. The patient suffered an unusually stressful life. In 1914, she emigrated from Germany to the United States accompanied by a young daughter. The child's father did not follow them for 15 years. Soon after her arrival the flexor tendon of the left fourth finger was accidentally severed. Initially sensation was absent from the palmar aspect of the fourth finger for several weeks. Following the injury she never was able to use the finger in a purposeful manner. She wore a ring on the affected finger from before the injury until age 63 when her husband died of cancer.

This clinical summary is presented primarily as an example of a lack-of-use situation in which disruption of information loops has probably affected the circulation, temperature, and perhaps electrophysical properties of a finger, having spared it from the rheumatoid and osteo-arthritic changes which developed in the other fingers.

### Experimental Studies

For some years experimental polyarthritis in rats has been produced by the injection of adjuvant. Pearson and Wood (1959, 1963) have studied such experimental arthritis from several points of view and have incidentally noted a distribution difference in joints affected, varying with the strain of rats employed. They also noted that some individual digits were spared arthritic involvement. Ward and Jones (1962) and Jones and Ward (1963) described a readily reproducible adjuvant-induced polyarthritis in rats by use of a mixture of *Mycobacterium butyricum* in oil, without emulsifier or saline solution. In their experience, the rather small amount (0.6 mg. dry heat-killed *M. butyricum* in 0.1 ml. oil) injected intradermally into the tail, gave polyarthritis in all of their test animals. Arthritis likewise appeared when the tails were removed, proximal to the injection site 2 hours after the injection.

We employed the method of Ward and Jones and observed the same sequence of systemic reaction and subsequent arthritis. In this experimental situation we also observed no cyclical variation in the extent of arthritic involvement. In the Sprague-Dawley and Holtzman strains, the ankle joints were quite evenly involved by arthritis in the control rats.

Using this model of experimental polyarthritis, we have attempted to induce paralysis and trauma of the rat limbs so as to study possible variations in distribution of joint involvement, time of appearance, and extent of arthritic change following injection of

adjuvant. Thus far we have not successfully produced hemiplegia by radiation or surgical damage to the brain.

It is recognized, of course, that these experimental conditions in rats may not produce patterns of joint involvement analogous to the arthritides in man. Differences may particularly obtain in relation to the psycho-physical organization of the body image as well as to other levels of organization, control, rhythm, and timing.

### Materials and Methods

Male rats of the Sprague-Dawley and Holtzman strains were used. They were fed Purina Chow® and water *ad libitum* and caged individually. Experimental stress was applied in the interval between 9 a.m. and 1 p.m. Conditioning was affected in each experiment and then 4 to 7 days later, at weights of 100 to 200 g., 0.6 to 0.9 mg. *Mycobacterium butyricum* (Difco®) heat-killed, suspended, and shaken in 0.1 to 0.15 ml. Squibb® auto-claved mineral oil was injected intradermally-subcutaneously into the tail. In two of the experiments, 2 hours after the inoculation, the tails were severed proximal to the injection site. Amputation of the tail did not affect the time of onset, extent, or severity of the experimental arthritis.

In the sciatic nerve section studies, 5 mm. of nerve were removed high up the thigh. In the fracture experiments, mid-thigh open fracture of the femur was performed surgically and 5 mm. of bone removed. In the cord damage study, dorso-lateral cord damage was produced surgically after laminectomy at the level of the first lumbar vertebra.

For the oscillating current experiment a pulse generator was constructed with a current similar to that described by Smith, Goodwin, Fowler, Smith, and Volpitta (1961). The apparatus could deliver 20 ma. each of D.C. and A.C. current through one lead. The oscillating current could be produced as a rectangular wave of 1 to 2 msec. duration, with oscillations up to 180 c.p.s., all as monitored by an oscilloscope. For this experiment rats were immobilized and silver electrodes imbedded in polyfoam, kept wet with concentrated saline, were applied, one to a shaved area of the sacral region of the back, and one to the foot pad of one foot. The positive pole was applied to the foot pad. First a direct current was quickly applied at 5 ma., then an alternating current was applied, gradually increasing to a peak of 10 ma. The alternating current was kept at 180 c.p.s. and 2/msec. duration. At this time 0.6 mg. *M. butyricum* in 0.1 ml. oil was injected into the tail intradermally-subcutaneously. After 2 hours the tails were severed proximal to the injection site and the current turned off.

Since the incubation period of this type of adjuvant arthritis is known to be from 9 to 23 days after the injection of adjuvant, the animals were observed for from 30 to 60 days. During the period from 9 to 18 days following injection the animals were inspected every day.

## Experimental Observations

### Sciatic Nerve Section Studies

- (A) Fifteen rats, average weight 199 g. (twelve of fifteen developed adjuvant arthritis) had unilateral sciatic nerve section, and 7 days later were injected with 0.9 mg. *M. butyricum* in 0.15 ml. oil, and were observed for 60 days following injection. Of the twelve which developed arthritis, two showed equal distribution of arthritis in all extremities, one had more severe arthritis in the ankle of the operated leg, and in six the arthritis appeared 2 to 3 days earlier and was more extensive in the unoperated hind leg, although arthritis did appear in the operated limb as well as in the forelegs. Three showed no arthritic change in the operated limb but had uniform distribution of arthritis in the other three limbs.
- (B) Twelve rats, average weight 140 g. (ten of twelve developed adjuvant arthritis) had unilateral sciatic nerve section, and 4 days later were injected with 0.6 mg. *M. butyricum* in 0.1 ml. oil, and were observed for 30 days following injection. Seven showed arthritis sooner by 1 or 2 days and more severely in the ankle of the unoperated leg; in three arthritis developed uniformly in all four extremities.
- (C) Eleven rats, average weight 119 g. (nine of eleven developed adjuvant arthritis) had unilateral sciatic nerve section, and 7 days later were injected with 0.6 mg. *M. butyricum* and 0.1 ml. oil, and were observed for 45 days. In four the arthritis developed first and was more severe in the ankle of the unoperated hind leg, in four the arthritis was uniformly distributed and in one more extensive arthritis developed in the ankle of the operated leg.
- (D) Sixteen rats, average weight 135 g., acting as controls (ten of sixteen developed adjuvant arthritis) were given a sham operation 7 days after the injection of 0.6 mg. *M. butyricum* in 0.1 ml. oil. Of the ten which developed arthritis, eight showed an equal distribution and uniformity in the extent of the arthritis, one showed a slightly more extensive arthritis in the operated leg, and one in the unoperated leg.

TOTAL OF OBSERVATIONS: In these experimental studies 31 of 38 animals developed arthritis. Three showed no arthritis in the operated leg, in seventeen the arthritis appeared first and developed more markedly in the ankle of the unoperated hind leg, in nine the arthritis was similar in onset and extent in both hind legs, and in two the arthritis was more severe in the ankle of the operated leg. Thus, in twenty of the 31 arthritic rats, prior section of one sciatic nerve appeared to delay the onset and diminish the severity of adjuvant arthritis in the operated limb.

### Fracture of Femur Studies

- (A) Fourteen rats, average weight 140 g. (seven of fourteen showed adjuvant arthritis), 7 days after surgical fracture of the femur were injected with 0.6 mg. *M. butyricum* in 0.1 ml. oil. Two rats showed uniform distribution of arthritis and in five the arthritis developed first and became more severe in the ankle of the unoperated leg.
- (B) Twelve rats, average weight 150 g., had surgical section of one femur, tantalum foil being placed between the bone ends, 7 days later they were injected with 0.6 mg. *M. butyricum* in 0.1 ml. oil. In two the arthritis developed more severely in the ankle of the unoperated leg, in two the arthritis was more severe on the operated side, two had uniform distribution of arthritis, and one had no clinical evidence of arthritis. The remaining five rats had an identical sequence of events; 14 days after the injection, arthritis appeared in both ankles but was definitely more severe in the ankle of the unoperated leg. By 22 days the arthritis in both ankles appeared the same and at the same time a slight arthritis appeared in the wrists. In 25 days the arthritis was much worse in the wrist on the side of the unoperated leg, and by 29 days the arthritis had become generally severe and appeared to be the same in both wrists and both ankles.
- (C) Five rats, average weight 150 g., acting as controls (all five developed adjuvant arthritis) were injected with 0.6 mg. *M. butyricum* in 0.1 ml. oil. All developed arthritis of the ankles of the hind legs uniformly in time and degree.

TOTAL OF OBSERVATIONS: In these experimental studies eighteen of 26 rats developed arthritis. Among these twelve showed arthritis sooner and more extensively in the ankle of the unoperated hind leg, in four the arthritis was uniform in onset and distribution, and two showed more extensive arthritis in the ankle of the operated limb. Observations were continued for 60 days after injection.

### Spinal Cord Studies

Twelve rats, average weight 117 g. (six of twelve developed adjuvant arthritis) were injected with 0.6 mg. *M. butyricum* in 0.1 ml. oil 4 days after operation.

- (A) *Partial paralysis of one leg* (three of seven showed arthritis).—All three animals showing arthritis had more severe joint involvement in the paralysed leg.
- (B) *Paralysis of both legs* (one of three showed arthritis).—One developed arthritis to the same extent bilaterally; two showed no evidence of arthritis.
- (C) *Flaccid paralysis in one leg*.—Two developed arthritis more extensively in the ankle of the paralysed leg.

- (D) Five rats, average weight 110 g., acting as controls (five of five developed arthritis) were subjected to laminectomy without cord damage, 4 days later they were injected with 0.6 mg. *M. butyricum* in 0.1 ml. oil. Arthritis developed in the ankles of the hind legs uniformly in time and degree.

**TOTAL OF OBSERVATIONS:** Three arthritic rats showed more severe arthritis in the paralysed hind limb; one rat with bilateral hind limb paralysis experienced arthritis to the same extent in each affected limb; two rats with flaccid paralysis developed more extensive arthritis in the affected limb. Observations were continued for 30 days after injection.

#### *Oscillating and Direct Electric Current Study*

- (A) Thirteen rats, average weight 171 g. (five of thirteen developed adjuvant arthritis) were subjected to a mixed current, as described above, for 2 hrs. After the first 10 min. they were injected with 0.6 mg. *M. butyricum* in 0.1 ml. oil. At the end of 2 hrs the tails were severed proximal to the injection site. The five rats which developed adjuvant arthritis showed a more extensive involvement in the ankle of the leg to which the current had been applied. Observations were continued for 45 days.

In Fig. 2 the deformity of the ankle and foot after sciatic nerve section is shown.



Fig. 2.—Deformity of foot and ankle following sciatic nerve section in a normal rat.

In Fig. 3 (opposite) a severe example of ankle arthritis on the leg with the intact sciatic nerve is illustrated. Slight evidence of toe arthritis is noted on the operated hind leg. In Fig. 4 (opposite) deformity and severe late arthritic changes are shown by x-ray in the ankle and foot of the intact limb, as contrasted to the lesser involvement of the operated side.

#### **Discussion**

Our experimental observations parallel those of Ward and Jones (1964) that adjuvant arthritis with *Mycobacterium butyricum* in oil alone showed no cyclical change and tended to evolve steadily with uniform distribution to the joints. On this firm basis our experimental results suggest that control factors in regard to distribution, severity, and timing of arthritis may partially reside in the integrity of complete use function and nerve-vascular function.

In the single patient described, several considerations may be entertained with regard to the sparing effect of tendon section. It is to be noted that the spared finger did have demonstrable circulatory changes. Subjectively, the patient reported diminished sensation to light touch and pin prick over the volar aspect of the left fourth finger. Complete motor nerve-to-muscle-to-perception function was lacking, and it is thus possible that the so-called body image of the finger had been altered. This high level control disturbance may have helped to prevent the development of osteo-arthritis and probable rheumatoid arthritis in this finger through local conditioning. One may also consider such a notion in hemiplegic patients as well as in the patient reported by Haddad (1963), who used her arm in spite of non-union of a fractured humerus. It may be that in the human, body image of function plays a leading role in some cases while other control factors are subservient. This would agree with the fact that in man there is much more encephalization and brain hemisphere differentiation function than in lower animals.

Our experimental findings in rats suggest also that the presence of fully functioning nerves in the limb are necessary for the natural distribution, intensity, and timing of the development of adjuvant arthritis. Fracture and attendant healing sequences may change both local conditions and functional awareness. Electro-physical properties may change as suggested by Becker (1961). The rats which were conditioned by various types of trauma did use their legs after a fashion but were handicapped in various ways from making full use of their paws and lower legs.

It is fairly clear that in most of our experimental rats the development of arthritis was delayed in the ankle of the leg in which the sciatic nerve was cut before inoculation. Current experimental studies suggest that when both the sciatic and saphenous nerves are severed (the latter having more sensory input) adjuvant arthritis is more severe in the ankle of the operated leg. This latter finding parallels those of our preliminary studies of the relationship between cord damage and paralysis and arthritis.

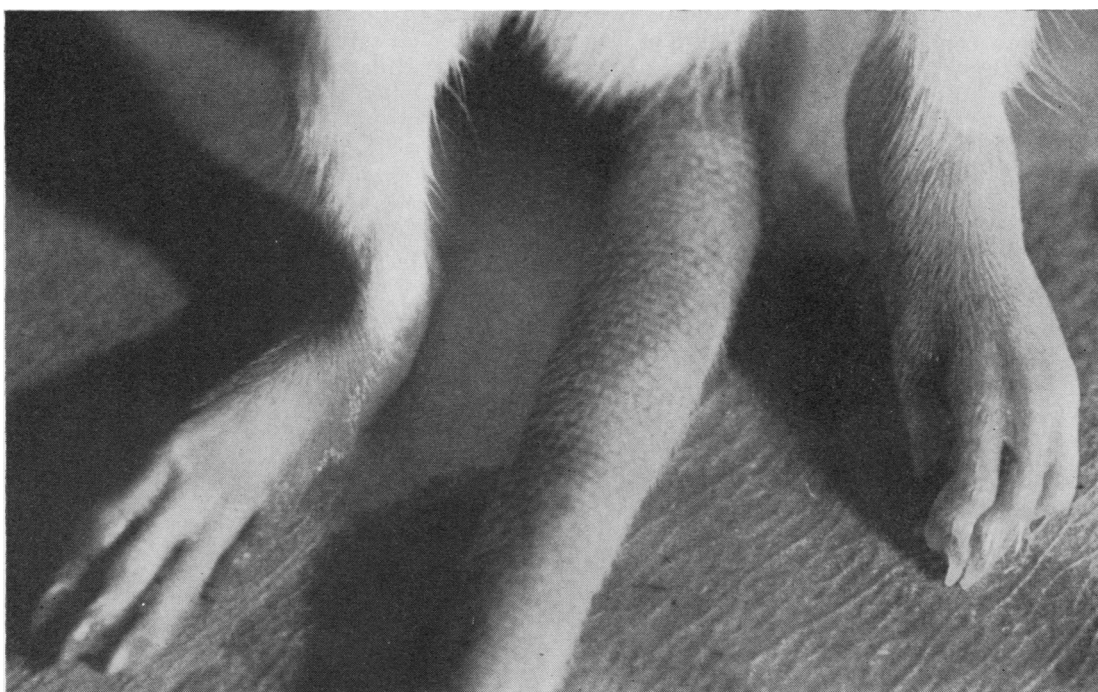


Fig. 3.—Example of severe arthritis in ankle of limb with intact sciatic nerve. Slight toe arthritis is seen on the side with sciatic nerve section.

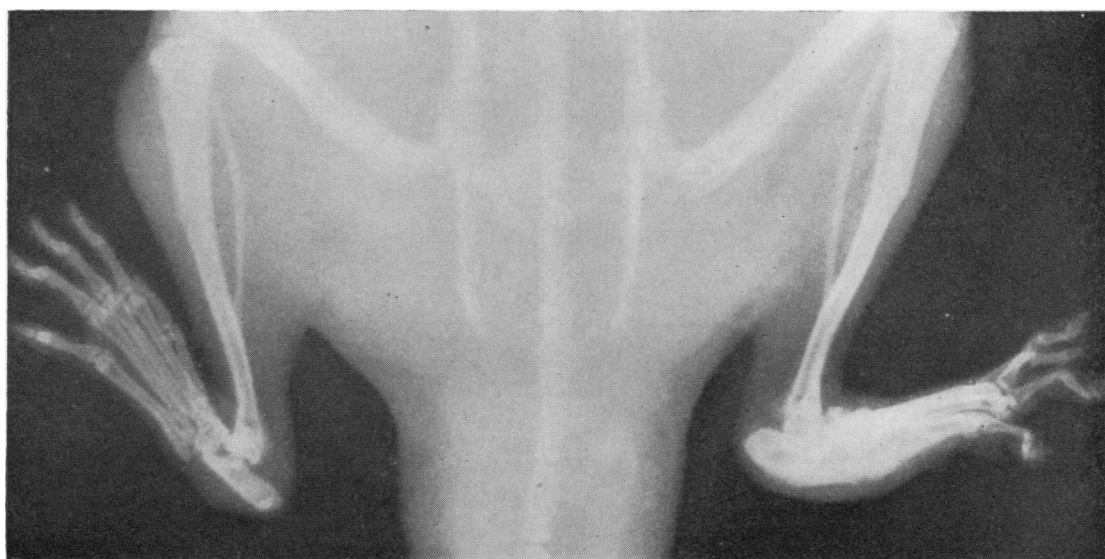


Fig. 4.—Severe late arthritic change involving the ankle and foot of the intact limb contrasted with a less extensive involvement of the limb with sciatic nerve section.



Since the course of experimental arthritis was thus apparently altered by procedures which interrupted the integrity of the functional information loops, we were led to study the effects of altering the information loops by externally applied electric currents.

We attempted to anaesthetize a single limb, employing a mixture of both oscillating and direct electric currents as suggested by Anan'ev, Golubeva, Gurova, Kaschevskaia, Levitskaia, and Khudyi; (1957) and Smith, Gramling, Smith, and Volpito (1961). Application of this current mixture with the positive pole on the foot pad for 2 hrs after inoculation of *M. butyricum* appeared to augment the arthritis in the limb. Among the possible explanations are the following:

- (1) Migration of cells and fluid to the site of application of the positive pole, as demonstrated by Carey and Lepley (1962).
- (2) Alteration of distribution of injected adjuvant.
- (3) Alteration of local conditioning by the mixed electric current alerting the rat to greater awareness of the limb.

A control system of possible primitive significance in regard to environment was hypothesized by Becker, Bachman, and Friedman (1962), who measured changes in direct current potentials between chlorided silver electrodes placed on various parts of the body and interpreted the patterns found as an electrodynamic field\* over the peripheral nervous system pattern having basic significance to the organism. They believed these currents to be constantly circulating on the body surface, like brain waves, making a primitive data transmission network. Becker (1961) found, that after fracture in an amphibian limb, there was a sharp drop from negative to positive polarity over the injury site, and that during a 15-day healing period there was a gradual return to normal. He thought that this observation of electrical change represented a field influencing the site of injury, possibly causing accumulation of cells of a type bearing specific electrical charges at points having specific electrical potentials.

Becker and others (1962) discovered that the small currents on the body surface, in contrast to the nerve potentials themselves, are influenced by external magnetism, barometric pressure, temperature, and light. These weather factors have long

been associated with variations in arthritic symptomatology. It was found that variations in microclimatic circumstances played a role in another type of sensitization phenomena, namely inhalation sensitization and asthma in guinea-pigs (Courtright and Courtright, 1945).

Moos and Solomon (1964a, b), Solomon and Moos (1964), and Solomon, Moos, Stone, and Fessel (1964) attempted to correlate emotional and psychic states with immunological competence. However, the notion of a unifying hierarchy of control and cause with variably stable and lasting information loops going beyond the classical description of psyche, nerve tissue, hormones, antibodies, and chemical entities may be of value here. Such a model could make more useful the many findings in the reports they cite. All of these could thus be combined into an organization of communication and control as in a cybernetic model.\*

Less inclusive cybernetic models are now becoming more common for the study of biological and psychological functions. Masturzo (1962) has been interested in using electrical information models containing threshold modifiers, changes in energy form by the use of transducers, and feedback loops, in order to analyse the biological information loops postulated for control of joint homeostasis. He believed that disturbances of biological loops may thus be analysed, particularly in regard to the vascular health of the joint, by relations to blood-vessel wall size and permeability. His theme is that "arthritis-rheumatism" may be regarded as a consequence of an information error along the circuit of neurovascular unity.

Another possible disturbance in the information loops could involve the memory pattern of body-image ordinarily sustained by continuous fully-integrated function; this would obviously exist in the hemiplegic patient and possibly to a lesser extent in patients with disunited nerve, tendon, and bones resulting in imperfect limb function and perception. In our experimental rats similar interruption of information loops may likewise have induced somewhat analogous situations. The sequence of development of adjuvant arthritis in five rats after femoral fracture appeared to indicate a sequence of arthritic involvement related to timed communication between the two sides of the body as well as superiorly-inferiorly (Katzman, 1964).

\* The term "field" may be considered merely as a field of influence and thus used loosely. It has been considered more scientifically in the sense of the electro-physical field properties of matter. Perhaps an even more appropriate and sophisticated notion, as stemming from present bio-physical research, should be that, as more processes are discovered in relation to cells, energy-entropy relationships, and electro-physical factors, these processes should all, at times, be considered only as cycling loops influencing behaviour. What influences what would then largely depend on the direction in which an observer might influence the loop.

\* The data supporting field theory have been accumulating over some years; yet the psyche has not yet been well connected. It is believed that a theoretical construction in the form of an hierarchical organization, of extremely low-energy, long-duration events (millions of years) at the top, and extremely short, large-energy events at the bottom may help in depicting information loops. Thus a model of the type described and analysed by Gregory and Kohnen (1959) could accelerate understanding of some classically-named and categorized entities and functions in medicine and biology.

Adjuvant arthritis, as induced by *Mycobacterium butyricum*, may be considered in relation to cybernetic information loops perpetuated by long-acting stable, low-energy patterns transmitted through genes. These bundles of events may reflect former responses to infection when viral or non-viable bacterial or chemical substances have stimulated them. The bacterial or chemical substances may themselves be correlated through past evolution in order to be able to arouse ancient response patterns. Rheumatoid arthritis may similarly represent reflections of remote-conditioning memory loops. Such theories may be useful, even though a virus may eventually be shown to induce the disease in genetically susceptible subjects.

These studies thus may raise important questions and suggest future avenues for research into the causation, timing, and control of various forms of arthritis. In man it is possible that higher orders of the nervous system and psyche may at times be necessary for instinctually projected manifestations of arthritis. In the rat, even though there is less encephalization and hemisphere differentiation, our studies reveal suggestive evidence of instinctual patterns of response which may transiently be interrupted to alter an ordinarily quite predictable pattern of adjuvant arthritis.

### Summary

A patient exhibiting the possible sparing effect of a previous unrepaired section of a flexor tendon on the development of a probable rheumatoid and a subsequent osteo-arthritis in the finger is described. Previously reported clinical examples of the arthritis-sparing effect of hemiplegia, nerve section, and bony non-union are reviewed.

An attempt was made to alter the course and extent of adjuvant arthritis in rats induced by *Mycobacterium butyricum* in oil, by a variety of procedures, including unilateral sciatic nerve section, femoral fracture, spinal cord injury, and application of a mixed oscillating and direct current over a hind limb.

In twenty of 31 arthritic rats prior section of one sciatic nerve appeared to delay the onset and diminish the extent of arthritis in the operated limb.

Twelve of the eighteen arthritic rats subjected to femur fracture developed arthritis later and less extensively in the injured than in the uninjured hind limb, in four the arthritis was the same each side, and in two arthritic changes were more severe in the fractured limb.

After surgical damage to the spinal cord, three rats showed a more extensive arthritis in a single

paralysed hind limb, one with both hind limbs paralysed showed a similar arthritis, and two others developed a more severe arthritis in the hind limb with flaccid paralysis.

The use of a mixture of oscillating and direct electric current with the positive pole on a hind foot pad in five rats was followed by the appearance of a more extensive arthritis in this limb.

### REFERENCES

- Anan'ev, M. G., Golubeva, I. V., Gurova, E. V., Kaschevskaia, L. A., Levitskaia, L. A., and Khudyi, Yu B. (1957). *Eksp. Khir.*, **4**, 3. (Trans. in *Anesthesiology* (1960), **21**, 215).
- Becker, R. O. (1961). *J. Bone Jt Surg.*, **43A**, 643.
- , Bachman, C. H., and Friedman, H. (1962). *N.Y. St. J. Med.*, **62**, 1169.
- Carey, L. C., and Lepley, D. Jr. (1962). *Surg. Forum*, **13**, 33.
- Courtright, L. J., and Courtright, A. B. (1945). *J. Allergy*, **16**, 146.
- Gregory, C. C. L., and Kohsen, A. (1959). "The O-Structure. An Introduction to Psychophysical Cosmology." Institute for the Study of Mental Images, Church Crookham, Hants.
- Haddad, J. (1963). To be published.
- Hench, P. S. (1940). *J. Amer. med. Ass.*, **115**, 2025.
- Jones, R. S., and Ward, J. R. (1963). *Arthr. and Rheum.*, **6**, 23.
- Katzman, R. (ed.) (1964). "Symposium: Sensory Evoked Response in Man." *Ann. N. Y. Acad. Sci.*, **112**, 1-546.
- Masturzo, A. (1962). "Atti del 1° Congresso Internazionale di Medicina Cibernetica, Napoli 2-5 Oct., 1960." Giannini, Napoli.
- Moos, R. H., and Solomon, G. F. (1964a). *Ann. rheum. Dis.*, **23**, 145.
- , — (1964b). *J. psychosomat. Res.*, **8**, 17.
- Nava, P. (1953). *Brasil-Méd.*, **67**, 318.
- Pearson, C. M., and Wood, F. D. (1959). *Arthr. and Rheum.*, **2**, 440.
- (1963). *Amer. J. Path.*, **42**, 73.
- Shannon, C. E., and Weaver, W. (1949). "Mathematical Theory of Communication." Univ. of Illinois Press, Urbana, Ill.
- Smith, R. H., Goodwin, C., Fowler, E., Smith, G. W., and Volpito, P. P. (1961). *Anesthesiology*, **22**, 163.
- , Gramling, Z. W., Smith, G. W., and Volpito, P. P. (1961). *Ibid.*, **22**, 970.
- Solomon, G. F., and Moos, R. H. (1964). *Arch. gen. Psychiat.*, **11**, 657.
- , —, Stone, G. C., and Fessel, W. J. (1964). *Angiology*, **15**, 362.
- Thompson, M., and Bywaters, E. G. L. (1962). *Ann. rheum. Dis.*, **21**, 370.
- Ward, J. R., and Jones, R. S. (1962). *Arthr. and Rheum.*, **5**, 557.
- , — (1964). Personal communication.



**Effet épargnant d'un déficit neurologique ou d'un traumatisme sur l'évolution de l'arthrite expérimentale chez le rat**

**RÉSUMÉ**

On décrit un malade manifestant un possible effet épargnant de la section non-réparée d'un tendon fléchisseur sur le développement d'une arthrite rhumatismale probable suivie d'ostéoarthrite du doigt. On passe en revue les exemples cliniques déjà rapportés de l'effet épargnant sur l'arthrite de l'hémiplégie, de la section nerveuse et de la pseudarthrose.

On a essayé de changer l'évolution et l'envergure de l'arthrite provoquée chez le rat par *Mycobacterium butyricum* en l'huile par un certain nombre de procédés, y compris la section unilatérale du nerf sciatique, la fracture fémorale, la lésion de la moelle épinière et l'application d'un courant mixte, oscillatoire et direct, à la patte postérieure.

Chez vingt rats sur trente-et-un la section d'un nerf sciatique semblait retarder le début de l'arthrite et réduire son envergure dans la patte opérée.

Chez douze sur dix-huit rats soumis à la fracture fémorale, l'arthrite apparut plus tard et fut moins grave dans la patte postérieure lésée que dans l'autre, chez quatre rats l'arthrite fut la même de deux côtés et chez deux d'entre eux les altérations arthritiques furent plus sévères dans la patte cassée.

Après la lésion chirurgicale de la moelle épinière trois rats accusèrent une plus grave arthrite dans la seule patte postérieure paralysée, un rat dont les deux pattes postérieures étaient paralysées accusa une similaire et deux autres développèrent une arthrite plus sévère dans la patte de derrière atteinte de paralysie flaccide.

L'application à cinq rats d'un mélange de courants électriques oscillatoire et direct, avec le pôle positif touchant une patte de derrière, fut suivie d'une arthrite plus sévère dans cette patte.

**Efecto ahorrativo de un déficit neurológico o de un traumatismo sobre la evolución de la artritis experimental en la rata**

**SUMARIO**

Se describe un enfermo manifestando un posible efecto ahorrativo de la sección sin reparar de un tendón flexor sobre el desarrollo de una artritis reumatoide probable seguida de una osteoartritis del dedo. Se pasa revista a los ejemplos clínicos ya relatados del efecto ahorrativo sobre la artritis de la hemiplegia, de la sección nerviosa y de la seudartrosis.

Se trató aquí de modificar la evolución y la severidad de la artritis provocada en la rata por *Mycobacterium butyricum* en suspensión oleosa con varios procedimientos, incluyendo la sección unilateral del nervio ciático, la fractura femoral, la lesión del cordón espinal y la aplicación de corrientes oscilante y directa a la pata trasera.

En veinte de treinta y un ratas la sección de un nervio ciático pareció retardar el comienzo y disminuir la severidad de la artritis en la pata operada.

De dieciocho ratas sometidas a la fractura del fémur, doce desarrollaron la artritis más tarde y menos extendida en la pata trasera injuriada, en cuatro la artritis fué igual en ambas patas y en dos la fué más grave en la pata rota.

Después de dañar quirúrgicamente el cordón espinal, tres ratas acusaron una artritis más grave en la pata trasera paralizada, una rata con ambas patas paralizadas acusó una artritis similar y otras dos desarrollaron una artritis más grave en la pata trasera con parálisis flácida.

Variaciones de corriente eléctrica directa y oscilante, con el polo positivo aplicado a una pata trasera de cinco ratas fueron seguidas de una artritis más severa en esta pata.